Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-15. (Canceled)

16. (New) A herpes simplex virus with a genome that comprises (i) an expressible non-herpes simplex virus nucleotide sequence encoding a desired protein and (ii) an alteration, relative to wild type, in the γ34.5 gene.

17. (New) The herpes simplex virus of claim 16, wherein both copies of said γ34.5 gene are altered, relative to wild type.

18. (New) The herpes simplex virus of claim 16, further comprising at least one further gene alteration, relative to wild type.

19. (New) The herpes simplex virus of claim 18, wherein said at least one further gene alteration is in the ribonucleotide reductase gene.

20. (New) The herpes simplex virus of claim 16, wherein said herpes simplex virus is G207.

21. (New) The herpes simplex virus of claim 16, wherein said protein is a cytokine.

22. (New) The herpes simplex virus of claim 16, wherein said virus is targeted to a tumor cell of non-nervous tissue origin.

23. (New) The herpes simplex virus of claim 22, wherein said tumor cell is a neural tumor cell.

24. (New) The herpes simplex virus of claim 16, wherein said virus is targeted to a specific tumor type with a tumor cell-specific promoter.

25. (New) The herpes simplex virus of claim 24, wherein said promoter is nestin promoter.

26. (New) The herpes simplex virus of claim 24, wherein said promoter is basic fibroblast growth factor promoter.

27. (New) The herpes simplex virus of claim 24, wherein said promoter is epidermal growth factor promoter.

28. (New) The herpes simplex virus of claim 16, wherein an essential viral gene product of said virus is under the control of a tumor cell-specific promoter rather than its own viral promoter.

29. (New) A composition comprising the herpes simplex virus of claim 16 and a pharmaceutically acceptable vehicle for said virus.

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A herpes simplex virus comprising (i) a mutation within the region of said virus corresponding to the BstEII - EcoNI fragment of the BamHI x fragment of the F strain of herpes simplex virus I, wherein said mutation consists essentially of a deletion of the BstEII - EcoNI fragment or a mutation within this fragment, and (ii) a further inactivating mutation in the γ 34.5 neurovirulence locus of said virus and/or an inactivating mutation elsewhere in the genome of said virus.

2. (Currently Amended) The virus of claim 1, wherein said virus comprises ~~further comprising~~ an inactivating mutation in the γ34.5 neurovirulence locus of said virus.

3. (Currently Amended) The virus of claim 1, wherein said virus comprises ~~further comprising~~ an inactivating mutation in the γ34.5 neurovirulence locus of said virus and an inactivating mutation in the ICP6 locus of said virus.

4. (Withdrawn) A herpes simplex virus comprising an inactivating mutation in the ICP47 locus of said virus, in the absence of an inactivating mutation in the γ34.5 neurovirulence locus of said virus.

5. (Currently Amended) The virus of claim 1 or 4, wherein said virus comprises ~~further comprising~~ an inactivating mutation in the ICP6 locus of said virus.

6. (Withdrawn) A method of inducing a systemic immune response to cancer in a patient, said method comprising administering to said patient a herpes virus comprising an inactivating mutation in the ICP47 locus of said herpes virus.

7. (Withdrawn) The method of claim 6, wherein said herpes virus is administered to a tumor of said patient.

8. (Withdrawn) The method of claim 6, wherein said patient has or is at risk of developing metastatic cancer.

9. (Withdrawn) The method of claim 6, wherein said inactivating mutation in the ICP47 locus of said herpes virus is in the BstEII - EcoNI fragment of the BamHI x fragment of said virus.

10. (Withdrawn) The method of claim 6, wherein said herpes virus further comprises an inactivating mutation in the γ34.5 neurovirulence locus of said herpes virus.

11. (Withdrawn) The method of claim 6, wherein said herpes virus further comprises an inactivating mutation in the ICP6 locus of said herpes virus.

12. (Withdrawn) The method of claim 6, wherein said herpes virus further comprises an inactivating mutation in the γ34.5 neurovirulence locus of said herpes virus and an inactivating

mutation in the ICP6 locus of said herpes virus.

13. (Withdrawn) A herpes virus comprising a first mutation that inactivates the γ34.5 neurovirulence locus of said virus and a second mutation that results in early expression of US11, in the absence of an ICP47-inactivating mutation in the BamHI x fragment of said virus.

14. (Withdrawn) The virus of claim 13, wherein said virus comprises a promoter inserted upstream from said US11 gene, resulting in said early expression.

15. (Withdrawn) The virus of claim 13, wherein said virus comprises a US11 gene under the control of an early-expressing promoter inserted into the genome of said virus.

16. (Withdrawn) The virus of claim 13, wherein said virus comprises a mutation that results in downregulation of ICP47 expression, in the absence of a mutation in the BamHI x fragment of said vector.

17. (Withdrawn) The virus of claim 16, wherein said downregulation of ICP47 expression is due to a deletion in, or inactivation of, the ICP47 promoter.

18. (Withdrawn) The virus of claim 16, wherein said virus encodes ICP47 that is fused with a peptide that prevents functional expression of ICP47.

19. (Withdrawn) A herpes virus comprising a first mutation that inactivates the γ34.5 neurovirulence locus of said virus and a second mutation that results in downregulation of ICP47 expression, in the absence of a mutation in the BamHI x fragment of said virus.

20. (Withdrawn) The virus of claim 19, wherein said downregulation of ICP47 expression is due to a deletion in, or inactivation of, the ICP47 promoter.

21. (Withdrawn) The virus of claim 19, wherein said virus encodes ICP47 that is fused with a peptide that prevents functional expression of ICP47.

22. (Withdrawn) The virus of claim 13 or 19, further comprising an additional mutation to prevent reversion to wild type.

23. (Withdrawn) The virus of claim 22, wherein said additional mutation is in the ICP6 locus.

24. (Original) The virus of claim 1, 4, 13, or 19, further comprising sequences encoding a heterologous gene product.

25. (Original) The virus of claim 24, wherein said heterologous gene product comprises a vaccine antigen or an immunomodulatory protein.

26. (Withdrawn) The virus of claim 13 or 19, wherein said virus is a herpes simplex virus.

27. (Original) The virus of claim 1, 4, or 26, wherein said virus is a herpes simplex-1 virus.

28. (Original) A pharmaceutical composition comprising the virus of claim 1, 4, 13, or 19 and a pharmaceutically acceptable carrier, adjuvant, or diluent.

29. (Withdrawn) A method of treating cancer in a patient, said method comprising administering the pharmaceutical composition of claim 28 to said patient.

30. (Withdrawn) A method of immunizing a patient against an infectious disease, cancer, or an autoimmune disease, said method comprising administering the pharmaceutical composition of claim 28 to said patient.

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AMENDMENT OF THE CLAIMS

This listing replaces all prior versions of the claims in this application.

1-34. (Canceled)

35. (Currently amended) A herpes simplex virus (HSV) that infects tumor cells but that does not spread in normal cells, with a genome comprising (i) at least one expressible nucleotide sequence encoding at least one immune modulator selected from the group consisting of IL-12 and GM-CSF and (ii) a mutation in the γ34.5 gene.

36. (Previously Presented) The HSV of claim 35, wherein both copies of said γ34.5 gene are mutated.

37. (Previously Presented) The HSV of claim 35, wherein said HSV further comprising at least one further gene mutation.

38. (Previously Presented) The HSV of claim 35, wherein said at least one further gene mutation is in ribonucleotide reductase.

39. (Previously Presented) The HSV of claim 35, wherein said HSV is G207.

40.-42. (Canceled)

43. (Previously Presented) The HSV of claim 35, wherein the tumor cells are of a type selected from the group consisting of astrocytoma, oligodendroglioma, meningioma, neurofibroma, glioblastoma, ependymoma, Schwannoma, neurofibrosarcoma, and medulloblastoma.

44. (Previously Presented) A composition comprising the HSV of claim 35 and a pharmaceutically acceptable vehicle for said HSV.

45. (New) The HSV of claim 35, wherein said immune modulator is IL-12.

46. (New) The HSV of claim 35, wherein said immune modulator is GM-CSF.